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Mouse melanocortin-4 receptor gene 5′-flanking region imparts cell specific expression in vitro

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Abstract

Weight homeostasis is exquisitely sensitive to changes in the abundance of melanocortin-4 receptor (MC4-R). To begin to understand the factors that regulate MC4-R gene expression, we determined there are no introns in the gene, there are multiple starts of transcription, and a cluster of 3′ ends. A series of MC4-R-luciferase gene reporter chimerics was developed and transfected into cell lines expressing (UMR106; GT1-7; HEK293) and not expressing (Neuro 2A) endogenous MC4-R mRNA. The longest construct, which includes a 3.3 kb 5′-flanking, 425 bp 5′-untranslated (UTR) and 1852 bp 3′-flanking, significantly increased luciferase reporter gene expression 24-, 13-, and 3-fold compared to pGL3-basic when expressed in HEK293, UMR106, and GT1-7 cells, respectively. Deletion analysis of mMC4-R 5′-flanking cDNA identified full mMC4-R promoter activity within 178 bp upstream of the

major start of transcription. The mMC4-R gene structure and reporter chimerics provide a fundamental framework for the identification of specific factors regulating MC4-R gene expression.



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Keywords

Melanocortin-4 receptor; Gene structure; Promoter activity

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